

KLOR-CON M10 - potassium chloride tablet, extended release

KLOR-CON M20 - potassium chloride tablet, extended release

Apace Packaging LLC

MICRO-DISPERSIBLE

TECHNOLOGY®

DESCRIPTION

Klor-Con® M20 is an immediately dispersing extended-release oral dosage form of potassium chloride containing 1500 mg of microencapsulated potassium chloride, USP equivalent to 20 mEq of potassium in a tablet.

Klor-Con® M15 is an immediately dispersing extended-release oral dosage form of potassium chloride containing 1125 mg of microencapsulated potassium chloride, USP equivalent to 15 mEq of potassium in a tablet.

Klor-Con® M10 is an immediately dispersing extended-release oral dosage form of potassium chloride containing 750 mg of microencapsulated potassium chloride, USP equivalent to 10 mEq of potassium in a tablet.

These formulations are intended to slow the release of potassium so that the likelihood of a high localized concentration of potassium chloride within the gastrointestinal tract is reduced.

Klor-Con® M is an electrolyte replenisher. The chemical name of the active ingredient is potassium chloride, and the structural formula is KCl (molecular weight: 74.55). Potassium chloride, USP occurs as a white, granular powder or as colorless crystals. It is odorless and has a saline taste. Its solutions are neutral to litmus. It is freely soluble in water and insoluble in alcohol.

Klor-Con® M is a tablet formulation (not enteric coated or wax matrix) containing individually microencapsulated potassium chloride crystals which disperse upon tablet disintegration. In simulated gastric fluid at 37°C and in the absence of outside agitation, Klor-Con® M begins disintegrating into microencapsulated crystals within seconds and completely disintegrates within one minute. The microencapsulated crystals are formulated to provide an extended release of potassium chloride.

Inactive Ingredients: croscarmellose sodium, ethylcellulose and microcrystalline cellulose.

CLINICAL PHARMACOLOGY

The potassium ion is the principal intracellular cation of most body tissues. Potassium ions participate in a number of essential physiological processes including the maintenance of intracellular tonicity, the transmission of nerve impulses, the contraction of cardiac, skeletal and smooth muscle and the maintenance of normal renal function.

The intracellular concentration of potassium is approximately 150 to 160 mEq per liter. The normal adult plasma concentration is 3.5 to 5 mEq per liter. An active ion transport system maintains this gradient across the plasma membrane.

Potassium is a normal dietary constituent and under steady state conditions the amount of potassium absorbed from the gastrointestinal tract is equal to the amount excreted in the urine. The usual dietary intake of potassium is 50 to 100 mEq per day.

Potassium depletion will occur whenever the rate of potassium loss through renal excretion and/or loss from the gastrointestinal tract exceeds the rate of potassium intake. Such depletion usually develops as a consequence of therapy with diuretics, primary or secondary hyperaldosteronism, diabetic ketoacidosis or inadequate replacement of potassium in patients on prolonged parenteral nutrition. Depletion can develop rapidly with severe diarrhea, especially if associated with vomiting.

Potassium depletion due to these causes is usually accompanied by a concomitant loss of chloride and is manifested by hypokalemia and metabolic alkalosis. Potassium depletion may produce weakness, fatigue, disturbances of cardiac rhythm (primary ectopic beats), prominent U-waves in the electrocardiogram, and in advanced cases, flaccid paralysis and/or impaired ability to concentrate urine.

If potassium depletion associated with metabolic alkalosis cannot be managed by correcting the fundamental cause of the deficiency, e.g., where the patient requires long term diuretic therapy, supplemental potassium in the form of high potassium food or potassium chloride may be able to restore normal potassium levels.

In rare circumstances (e.g., patients with renal tubular acidosis) potassium depletion may be associated with metabolic acidosis and hyperchloremia. In such patients potassium replacement should be accomplished with potassium salts other than the chloride, such as potassium bicarbonate, potassium citrate, potassium acetate or potassium gluconate.

INDICATIONS AND USAGE

BECAUSE OF REPORTS OF INTESTINAL AND GASTRIC ULCERATION AND BLEEDING WITH EXTENDED-RELEASE POTASSIUM CHLORIDE PREPARATIONS, THESE DRUGS SHOULD BE RESERVED FOR THOSE PATIENTS WHO CANNOT TOLERATE OR REFUSE TO TAKE LIQUID OR EFFERVESCENT POTASSIUM PREPARATIONS OR FOR PATIENTS IN WHOM THERE IS A PROBLEM OF COMPLIANCE WITH THESE PREPARATIONS.

1. For the treatment of patients with hypokalemia with or without metabolic alkalosis, in digitalis intoxication and in patients with hypokalemic familial periodic paralysis. If hypokalemia is the result of diuretic therapy, consideration should be given to the use of a lower dose of diuretic, which may be sufficient without leading to hypokalemia.
2. For the prevention of hypokalemia in patients who would be at particular risk if hypokalemia were to develop, e.g., digitalized patients or patients with significant cardiac arrhythmias.

The use of potassium salts in patients receiving diuretics for uncomplicated essential hypertension is often unnecessary when such patients have a normal dietary pattern and when low doses of the diuretic are used. Serum potassium should be checked periodically, however, and if hypokalemia occurs, dietary supplementation with potassium-containing foods may be adequate to control milder cases. In more severe cases, and if dose adjustment of the diuretic is ineffective or unwarranted, supplementation with potassium salts may be indicated.

CONTRAINDICATIONS

Potassium supplements are contraindicated in patients with hyperkalemia since a further increase in serum potassium concentration in such patients can produce cardiac arrest. Hyperkalemia may complicate any of the following conditions: chronic renal failure, systemic acidosis, such as diabetic acidosis, acute dehydration, extensive tissue breakdown as in severe burns, adrenal insufficiency or the administration of a potassium-sparing diuretic (e.g., spironolactone, triamterene or amiloride) (see **OVERDOSAGE**).

Extended-release formulations of potassium chloride have produced esophageal ulceration in certain cardiac patients with esophageal compression due to enlarged left atrium. Potassium supplementation, when indicated in such patients, should be given as a liquid preparation or as an aqueous (water) suspension of Klor-Con[®] M (see **PRECAUTIONS; Information for Patients** and **DOSAGE AND ADMINISTRATION** sections).

All solid oral dosage forms of potassium chloride are contraindicated in any patient in whom there is structural, pathological (e.g., diabetic gastroparesis) or pharmacologic (use of anticholinergic agents or other agents with anticholinergic properties at sufficient doses to exert anticholinergic effects) cause for arrest or delay in tablet passage through the gastrointestinal tract.

WARNINGS

Hyperkalemia (see **OVERDOSAGE**):—In patients with impaired mechanisms for excreting potassium, the administration of potassium salts can produce hyperkalemia and cardiac arrest. This occurs most commonly in patients given potassium by the intravenous route but may also occur in patients given potassium orally. Potentially fatal hyperkalemia can develop rapidly and be asymptomatic. The use of potassium salts in patients with chronic renal disease, or any other condition which impairs potassium excretion, requires particularly careful monitoring of the serum potassium concentration and appropriate dosage adjustment.

Interaction with Potassium-Sparing Diuretics—Hypokalemia should not be treated by the concomitant administration of potassium salts and a potassium-sparing diuretic (e.g., spironolactone, triamterene or amiloride) since the simultaneous administration of these agents can produce severe hyperkalemia.

Interaction with Angiotensin Converting Enzyme Inhibitors—Angiotensin converting enzyme (ACE) inhibitors (e.g., captopril, enalapril) will produce some potassium retention by inhibiting aldosterone production. Potassium supplements should be given to patients receiving ACE inhibitors only with close monitoring.

Gastrointestinal Lesions—Solid oral dosage forms of potassium chloride can produce ulcerative and/or stenotic lesions of the gastrointestinal tract. Based on spontaneous adverse reaction reports, enteric coated preparations of potassium chloride are associated with an increased frequency of small bowel lesions (40- 50 per 100,000 patients years) compared to extended-release wax matrix formulations (less than one per 100,000 patients years). Because of the lack of extensive marketing experience with microencapsulated products, a comparison between such products and wax matrix or enteric coated products is not available. Klor-Con[®] M is a tablet formulated to provide an extended rate of release of microencapsulated potassium chloride and thus to minimize the possibility of a high concentration of potassium near the gastrointestinal wall.

Prospective trials have been conducted in normal human volunteers in which the upper gastrointestinal tract was evaluated by endoscopic inspection before and after one week of solid oral potassium chloride therapy. The ability of this model to predict events occurring in usual clinical practice is unknown. Trials which approximated usual clinical practice did not reveal any clear differences between the wax matrix and microencapsulated dosage forms. In contrast, there was a higher incidence of gastric and duodenal lesions in subjects receiving a high dose of wax matrix extended-release formulation under conditions potassium chloride administered to fasted patients, in the presence of an anticholinergic drug to delay gastric emptying). The upper gastrointestinal lesions observed by endoscopy were asymptomatic and were not accompanied by evidence of bleeding (hemoccult testing). The relevance of these findings to the usual conditions (i.e., non-fasting, no anticholinergic agent, smaller doses) under which extended-release potassium chloride products are used is uncertain; epidemiologic studies have not identified an elevated risk, compared to microencapsulated products, for upper gastrointestinal lesions in patients receiving wax matrix formulations. Klor-Con[®] M should be discontinued immediately and the possibility of ulceration, obstruction or perforation considered if severe vomiting, abdominal pain, distention or gastrointestinal bleeding occurs.

Metabolic Acidosis: Hypokalemia in patients with metabolic acidosis should be treated with an alkalinizing potassium salt such as potassium bicarbonate, potassium citrate, potassium acetate or potassium gluconate.

PRECAUTIONS

General:

The diagnosis of potassium depletion is ordinarily made by demonstrating hypokalemia in a patient with a clinical history suggesting some cause for potassium depletion. In interpreting the serum potassium level, the physician should be aware that acute alkalosis *per se* can produce hypokalemia in the absence of a deficit in total body potassium while acute acidosis *per se* can increase the serum

potassium concentration into the normal range even in the presence of a reduced total body potassium. The treatment of potassium depletion, particularly in the presence of cardiac disease, renal disease or acidosis requires careful attention to acid-base balance and appropriate monitoring of serum electrolytes, the electrocardiogram and the clinical status of the patient.

Information for Patients:

Physicians should consider reminding the patient of the following:

To take each dose with meals and with a full glass of water or other liquid.

To take each dose without crushing, chewing or sucking the tablets. If those patients are having difficulty swallowing whole tablets, they may try one of the following alternative methods of administration:

a. Break the tablet in half and take each half separately with a glass of water.

b. Prepare an aqueous (water) suspension as follows:

1. Place the whole tablet(s) in approximately one-half glass of water (4 fluid ounces).
2. Allow approximately 2 minutes for the tablet(s) to disintegrate.
3. Stir for about half a minute after the tablet(s) had disintegrated.
4. Swirl the suspension and consume the entire contents of the glass immediately by drinking or by the use of a straw.
5. Add another one fluid ounce of water, swirl and consume immediately.
6. Then, add an additional one fluid ounce of water, swirl and consume immediately.

Aqueous suspension of Klor-Con[®] M Extended-release Tablets that is not taken immediately should be discarded. The use of other liquids for suspending Klor-Con[®] M Tablets is not recommended. To take this medicine following the frequency and amount prescribed by the physician. This is especially important if the patient is also taking diuretics and/or digitalis preparations. To check with the physician at once if tarry stools or other evidence of gastrointestinal bleeding is noticed.

Laboratory Tests:

When blood is drawn for analysis of plasma potassium it is important to recognize that artifactual elevations can occur after improper venipuncture technique or as a result of *in-vitro* hemolysis of the sample.

Drug Interactions:

Potassium-sparing diuretics, angiotensin converting enzyme inhibitors (see **WARNINGS**).

Carcinogenesis, Mutagenesis, Impairment of Fertility:

Carcinogenicity, mutagenicity and fertility studies in animals have not been performed.

Potassium is a normal dietary constituent.

Pregnancy:

Pregnancy Category C: Animal reproduction studies have not been conducted with Klor-Con[®] M. It is unlikely that potassium supplementation that does not lead to hyperkalemia would have an adverse effect on the fetus or would affect reproductive capacity.

Nursing Mothers:

The normal potassium ion content of human milk is about 13 mEq per liter. Since oral potassium becomes part of the body potassium pool, so long as body potassium is not excessive, the contribution of potassium chloride supplementation should have little or no effect on the level in human milk.

Pediatric Use:

Safety and effectiveness in pediatric patients have not been established.

ADVERSE REACTIONS

One of the most severe adverse effects is hyperkalemia (see **CONTRAINDICATIONS**, **WARNINGS** and **OVERDOSAGE**). There have also been reports of upper and lower gastrointestinal conditions including obstruction, bleeding, ulceration and perforation (see **CONTRAINDICATIONS** and **WARNINGS**).

The most common adverse reactions to oral potassium salts are nausea, vomiting, flatulence, abdominal pain/discomfort and diarrhea. These symptoms are due to irritation of the gastrointestinal tract and are best managed by diluting the preparation further, taking the dose with meals or reducing the amount taken at one time.

OVERDOSAGE

The administration of oral potassium salts to persons with normal excretory mechanisms for potassium rarely causes serious hyperkalemia. However, if excretory mechanisms are impaired or if potassium is administered too rapidly intravenously, potentially fatal hyperkalemia can result (see **CONTRAINDICATIONS** and **WARNINGS**). It is important to recognize that hyperkalemia is usually asymptomatic and may be manifested only by an increased serum potassium concentration (6.5-8.0 mEq/L) and characteristic electrocardiographic changes (peaking of T-waves, loss of P-waves, depression of S-T segment and prolongation of the QT-interval). Late manifestation includes muscle paralysis and cardiovascular collapse from cardiac arrest (9-12 mEq/L).

Treatment measures for hyperkalemia include the following:

1. Elimination of foods and medications containing potassium and of any agents with potassium sparing properties.
2. Intravenous administration of 300 to 500 mL/hr of 10% dextrose injection containing 10-20 units of crystalline insulin per 1,000 mL.
3. Correction of acidosis, if present, with intravenous sodium bicarbonate.
4. Use of exchange resins, hemodialysis or peritoneal dialysis.

In treating hyperkalemia, it should be recalled that in patients who have been stabilized on digitalis, too rapid a lowering of the serum potassium concentration can produce digitalis toxicity.

DOSAGE AND ADMINISTRATION

The usual dietary intake of potassium by the average adult is 50 to 100 mEq per day. Potassium depletion sufficient to cause hypokalemia usually requires the loss of 200 or more mEq of potassium from the total body store.

Dosage must be adjusted to the individual needs of each patient. The dose for the prevention of hypokalemia is typically in the range of 20 mEq per day. Doses of 40-100 mEq per day or more are used for the treatment of potassium depletion. Dosage should be divided if more than 20 mEq per day is given such that no more than 20 mEq is given in a single dose.

Klor-Con[®] M20 Tablet provided 1500 mg of potassium chloride equivalent to 20 mEq of potassium.

Klor-Con[®] M10 Tablet provided 750 mg of potassium chloride equivalent to 10 mEq of potassium.

Klor-Con[®] M Tablets should be taken with meals and with a glass of water or other liquid. This product should not be taken on an empty stomach because of its potential for gastric irritation (see **WARNINGS**).

Patients having difficulty swallowing whole tablets may try one of the following alternative methods of administration:

- a. Break the tablet in half and take each half separately with a glass of water.
- b. Prepare an aqueous (water) suspension as follows:
 1. Place the whole tablet(s) in approximately one-half glass of water (4 fluid ounces).
 2. Allow approximately 2 minutes for the tablet(s) to disintegrate.
 3. Stir for about half a minute after the tablet(s) had disintegrated.
 4. Swirl the suspension and consume the entire contents of the glass immediately by drinking or by the use of a straw.
 5. Add another one fluid ounce of water, swirl and consume immediately.
 6. Then, add an additional one fluid ounce of water, swirl and consume immediately.

Aqueous suspension of Klor-Con[®] M Extended-release Tablet that is not taken immediately should be discarded. The use of other liquids for suspending Klor-Con[®] M is not recommended.

HOW SUPPLIED

Klor-Con[®] M20 Extended-release Tablets, 1500 mg of potassium chloride (20 mEq of potassium) are available in bottles of 30 (NDC 15338-133-30). Klor-Con[®] M20 tablets are white, oblong, imprinted KC M20 and scored for flexibility of dosing.

Klor-Con[®] M10 Extended-release Tablets, 750 mg of potassium chloride (10 mEq of potassium) are available in bottles of 30 (NDC 15338-122-30). Klor-Con[®] M10 tablets are white, oblong, imprinted KC M10.

Storage Conditions: Keep tightly closed. Store at controlled room temperature, 15-30°C (59-86°F).

Manufactured by

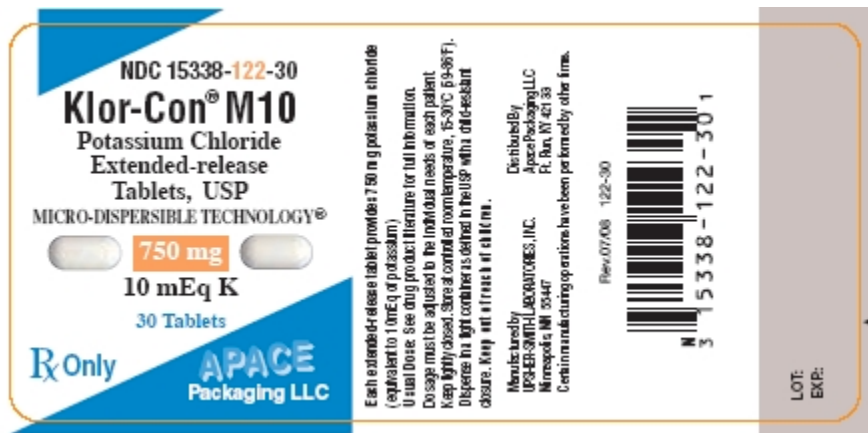
UPSHER-SMITH LABORATORIES, INC.

Minneapolis, MN 55447

US Patent 6,780,437

Certain manufacturing operations have been performed by other firms.

PRINCIPAL DISPLAY PANEL- 10 MEQ K



NDC 15338-122-30

Klor-Con® M10
Potassium Chloride
Extended-release
Tablets, USP
MICRO-DISPERSIBLE TECHNOLOGY®

750 mg
10 mEq K
30 Tablets
Rx Only

Each extended-release tablet provides 750 mg potassium chloride
(equivalent to 10mEq of potassium)

Usual Dose: See drug product literature for full information.

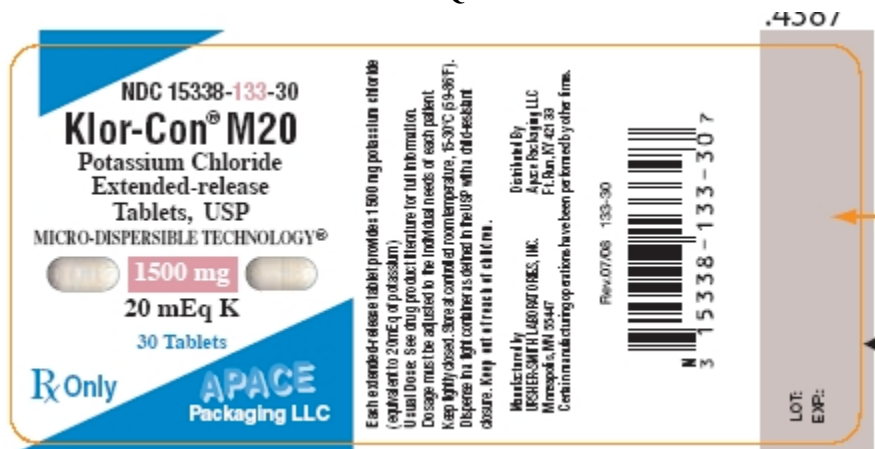
Dosage must be adjusted to the individual needs of each patient.

Keep tightly closed. Store at controlled room temperature, 15-30°C (59-86°F).

Dispense in a tight container as defined in the USP with a child-resistant closure. **Keep out of reach of children.**

Rev.07/08 122-30

PRINCIPAL DISPLAY PANEL- 20 MEQ K



NDC 15338-133-30

Klor-Con® M20
Potassium Chloride
Extended-release
Tablets, USP

MICRO-DISPERSIBLE TECHNOLOGY®

1500 mg

20 mEq K

30 Tablets

Rx Only

Each extended-release tablet provides 1500 mg potassium chloride

(equivalent to 20mEq of potassium)

Usual Dose: See drug product literature for full information.

Dosage must be adjusted to the individual needs of each patient.

Keep tightly closed. Store at controlled room temperature, 15-30°C (59-86°F).

Dispense in a tight container as defined in the USP with a child-resistant closure. **Keep out of reach of children.**

Rev.07/08 133-30